

WE CLAIM:

1. Folliculo stellate-derived growth factor in isolated form.

2. Folliculo stellate-derived growth factor of Claim 1 which is a dimeric protein having a molecular weight of approximately 43 kd, as determined by SS polyacrylamide electrophoresis under non-reducing conditions, and which
5 comprises at its N-terminus the amino acid sequence Ala-¹Pro-Met-Ala-Glu-Gly-Gly-Gln-Lys-Pro-His-Glu.

3. Folliculo stellate-derived growth factor of Claim 2 which further comprises an internal amino acid sequence, obtainable upon tryptic digestion, selected from the group consisting of:

5 Ser-Phe-Cys-Arg-Pro-Ile-Glu-Thr-Leu-Val-Ssp-Ile-Phe-Gln-Glu-Tyr-Pro-Asp-Glu-Ile; and

Ser-Phe-Cys-Arg-Pro-Ile-Glu-Thr-Leu-Val-Ssp-Ile-Phe-Gln-Glu-Tyr-Pro-Asp/Ile Glu.

4. A method of promoting the proliferation of endothelial cells which comprises applying to such cells a mitogenic amount of folliculo stellate-derived growth factor of Claim 1.

5. The method of Claim 4, wherein the endothelial cells are grown in cell culture.

6. A method of promoting vascular endothelialization which comprises applying to vascular surfaces of a host in need of such treatment an amount of follicular stellate-derived growth factor of Claim 1 sufficient to promote
5 endothelialization.

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7. The method of Claim 6, wherein the folliculo stellate-derived growth factor is applied post-operatively to vascular surfaces following balloon angioplasty.

8. The method of Claim 6, wherein the folliculo stellate-derived growth factor is applied to the surfaces of vasculature and/or the surfaces of vascular grafts during or prior to vascular graft surgery.

9. The method of Claim 6, wherein the folliculo stellate-derived growth factor is administered to a host following myocardial infarction.

10. A method of promoting wound healing which comprises administering to a wound an amount of the folliculo stellate-derived growth factor of Claim 1 sufficient to promote angiogenesis at the wound site.

11. A pharmaceutical composition comprising the folliculo stellate-derived growth factor of Claim 1 and pharmaceutically acceptable carrier vehicle.

12. A method for producing a substantially pure folliculo stellate-derived growth factor (FSdGF) in isolated form, which method comprises:

5 (a) providing a biological sample containing levels of FSdGF;

(b) extracting the solubilized portion of the sample;

(c) partially purifying the FSdGF from the extract using an aqueous salt-precipitation step;

10 (d) fractionating the purified extract using affinity chromatography employing heparin moieties linked

to an insoluble support as the stationary phase and employing a salt gradient mobile phase of increasing salt concentration;

15 (e) fractionating the extract using gel exclusion chromatography;

 (f) fractionating the sample using liquid chromatography; and optionally

 (g) purifying the extract using reverse-phase
20 high performance liquid chromatography.

13. The method of Claim 12 wherein in step (c) the aqueous salt precipitation uses ammonium sulphate.

14. The purified folliculo stellate-derived growth factor obtained by the method of Claim 12.

15. The folliculo stellate-derived growth factor in purified form which is a glycoprotein consisting essentially of two substantially homologous subunits each having a molecular weight of about 23,000 daltons.

16. The folliculo stellate-derived growth factor of Claim 1 which is effective in wound healing in a human being at a concentration of between about 10 picogram/milliliter and about 500 picogram/milliliter.

17. The method of Claim 12 wherein:

 in the partially purifying step the FSdGF is contacted with aqueous ammonium sulfate solution;

 in fractionating step (d) the heparin is attached
5 to sepharose; and

 in the purifying step (g) the reverse phase high performance liquid chromatography is conducted using

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18. The purified growth factor produced by the method of Claim 17.

20. The folliculo stellate-derived growth factor of Claim 19 having a molecular weight of about 43,000 da.

22. The folliculo stellate-derived growth factor of Claim 21 having a molecular weight of about 43 kDa.

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25. The folliculo stellate-derived growth factor of Claim 21 which under reducing conditions produces a substantially homologous dimer each unit having a molecular weight of about 23,000 daltons.

26. A method of obtaining a concentrated folliculo stellate-derived growth factor in isolated form, which method comprises:

5 (a) obtaining a biological liquid supernatant sample containing levels of FSdGF using the conditioning medium of a culture;

(b) fractionating the sample of step (a) using heparin moities linked to an insoluble support as the stationary phase and using a salt gradient mobile
10 phase of increasing salt concentration; and

(c) purifying the bioactive fraction of step (b) using gel electrophoresis.

27. The method of Claim 26 wherein in the fractionating step the growth factor elutes at a sodium chloride concentration of between about 0.6 and 1.0 Molar.

28. The method of Claim 27 wherein in the purifying step the gel is a suitable polyacrylamide.

29. The folliculo stellate-derived growth factor produced by the method of Claim 26 having a molecular weight of about 43,000 da.

30. A pharmaceutical composition comprising the folliculo stellate-derived growth factor produced by the method of Claim 26.

31. A pharmaceutical composition comprising the folliculo stellate-derived growth factor of Claim 21 and a pharmaceutically acceptable carrier vehicle.

32. The pharmaceutical composition of Claim 21 wherein the carrier vehicle is a parenteral carrier vehicle.

33. A method of obtaining a substantially pure folliculo stellate-derived growth factor (FSdGF) in

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isolated form, which method comprises:

5 (a) providing a biological sample containing levels of FSdGF;

(b) extracting the solubilized portion of the sample;

(c) partially purifying the FSdGF from the extract using an aqueous salt-precipitation step;

10 (d) fractionating the purified extract using affinity chromatography employing heparin moieties linked to an insoluble support as the stationary phase and employing a salt gradient mobile phase of increasing salt concentration;

15 (e) fractionating the extract using gel exclusion chromatography; and

(f) purifying the extract using reverse-phase high pressure liquid chromatography.

34. The purified folliculo stellate-derived growth factor obtained by the method of Claim 33.

35. The purified folliculo stellate-derived growth factor of Claim 35 having a molecular weight of between about 43,000 and 45,000 da.

36. A folliculo stellate-derived growth factor in purified form which is a glycoprotein consisting essentially of two substantially homologous subunits each having a molecular weight of about 23,000 daltons.

37. The folliculo stellate-derived growth factor of Claim 21 which is effective in wound healing in a human being at a concentration of between about 10

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picogram/milliliter and about 500 picogram/milliliter.

38. The method of Claim 33 wherein in step (f) the reverse phase high pressure liquid chromatography is performed using an aqueous acetonitrile gradient.

39. The method of Claim 33 which further includes:

(g) purifying the concentrated product of step (f) using reverse phase high performance liquid chromatography with an aqueous isopropanol gradient.

40. The folliculo-stellate-derived growth factor of Claims 20 having an N-terminus internal amino acid sequence of: Ala-Pro-Met-Ala-Glu-Gly-Gly-Gln-Lys-Pro-His-Glu-Val-Val-Lys-Phe-Met-Asp-Val-Tyr-Gln-(Arg)-Ser-Phe-X-Arg-Pro-Ile-Glu-Thr-Leu-(Val)-X-Ile-X-(Gln)-Glu-Tyr-(Pro)- wherein the amino acids in parenthesis are certain and the -X- indicates an amino acid of unknown identity.

41. A process for producing human endothelial cell growth factor comprising, providing a replicable expression vector capable of expressing the DNA sequence encoding human endothelial cell growth factor in a suitable host, transforming said host to obtain a recombinant host, and maintaining said recombinant host under conditions permitting expression of said endothelial cell growth factor - encoding cDNA sequence to produce endothelial cell growth factor.

42. The process according to claim 41 including the further step of recovering said endothelial cell growth factor.

43. The process according to claim 42 wherein said

expression vector is a bacteriophage.

44. The process according to claim 42 wherein said expression vector is plasmid.

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